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EXAMINER	
FETTEROLF, BRANDON J	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/761,150	ANDREU MORALES ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7,8,10,11 and 13-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,7,8,10,11 and 13-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to the Amendment

The Amendment filed on 2/21/2007 in response to the previous Non-Final Office Action (9/15/2006) is acknowledged and has been entered.

Claims 1-2, 4-5, 7-8, 10-11 and 13-18 are currently pending and under consideration.

Priority:

In reference to the prior office Non-Final Office Action wherein the Examiner has established a priority date of **1/20/2004** consistent with the instant application 10/761,150 because a certified copy of the international application and English translation of the international application have not been provided, see MPEP 1895.01, Applicants assert that following conversations with WIPO, it is believed that this request is not correct. In particular, Applicants assert that the present application is a PCT application entering national phase to which the provisions other than those relating to direct US national filings, apply. Thus, Applicants submit that where a PCT application enters the national phase (and as distinct from direct national applications) the overall structure of Article 27 and Rule 51bis-of "the national law applicable by the designated office may require"-shows the hierarchy of the Treaty over the national law/practive, with the Treaty allowing a national Office to require certain specific things in respect of a PCT national phase filing, but clearly defining very narrowly those instances. Concerning the priority document, Rule 17.2 specifically states that where the applicant has timely furnished the priority document to the International bureau, that bureau furnishes a copy of the priority document to the designated Office upon the specific request of that Office. No such office will ask the applicant himself to furnish it with a copy. Thus, Applicants assert that enclosed herewith is a sworn translations of the priority document, and respectfully submit that the claimed priority date of July 20, 2001 is perfected.

These arguments have been carefully considered, but are not found persuasive.

In the instant case, the Examiner recognizes that, contrary to Applicants assertions, the instant application is not an international application entering the U.S. national phase under 35 U.S.C. 371, but is a continuation of PCT application, PCT/ES02/00262, filed on 05/31/2002 under

35 U.S.C. 120 and claims priority under U.S.C. 119(a)-(d) as to Spanish Application Serial No. 200101710 (see specification, page 1). As such, to obtain benefit under 35 U.S.C. 120 and 365(c) of a prior international application designating the U.S., the continuing application must:

(A) include a specific reference to the prior international application (either in the application data sheet (37 CFR 1.76) or in the first sentence(s) of the specification),

(B) be copending with the prior international application, and

(C) have at least one inventor in common with the prior international application.

With regard to (A), the specific reference to the international application required under 35 U.S.C. 120 and 365(c) must either be contained in the first sentence(s) of the specification following the title or included in an application data sheet. 37 CFR 1.78(a)(2)(iii). The specific reference must identify the parent international application by international application number and international filing date and indicate the relationship of the applications (i.e., continuation, continuation-in-part, or division). See 37 CFR 1.78(a)(2)(i)) and MPEP § 201.11. An example of an appropriate first sentence of the specification is, for example, "This is a continuation of International Application PCT/EP2004/000000, with an international filing date of January 5, 2004, now abandoned." The required reference must be submitted within the time period provided by 37 CFR 1.78(a)(5)(ii). This time period is not extendable. A certified copy of the international application (and an English translation) of the international application may be required by the examiner to perfect the claim for benefit under 35 U.S.C. 120 and 365(c) if the international application did not originate in the United States and such is necessary, for example, where an intervening reference is found and applied in a rejection of one or more claims, *see* MPEP 1895.01 [R5]. (emphasis added) With regards to the submission of the sworn translation of the priority document, the Examiner has carefully reviewed Applicants 2/21/2007 submission and can not find any sworn translation of the priority document. Thus, the priority date of **1/20/2004** consistent with the instant application 10/761,150 is maintained.

Information Disclosure Statement

In reference to the prior office Non-Final Office Action wherein the Examiner noted that the information disclosure statement filed on 05/12/2005 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by

the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language, Applicants assert that three applications in Spanish have been noted and submission of a translation of the PCT application is enclosed herewith.

These arguments have been carefully considered, but are not found persuasive.

In the instant case, the Examiner has carefully reviewed Applicants 2/21/2007 submission, but could not find a translation of the PCT application. As such, the information disclosure statement filed on 05/12/2005 fails to comply with 37 CFR 1.98(a)(3) as set forth in the prior office action.

Rejections Maintained:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4-5, 7-8, 10-11 and 13-18 remain rejected under 35 U.S.C. 102(b) as being anticipated by Diaz et al. (J. Biol. Chem. 2000; 275: 26265-26276, *IDS*).

(Note: Due to the indefiniteness of the phrase "displacement equilibrium curve" in claim 1, see below, the claim will be interpreted as determining a displacement curve.)

Diaz et al. teach a method of providing a homogenous test for the detection of an antitumor substance in the paclitaxel binding site of microtubules, wherein said method is based on the combination of a target and a probe and comprises the following steps: adding a test substance or test substances to a solution of a target consisting of microtubules and a fluorescent probe bound to the target; determining a displacement curve of the probe from the target by the test substance, wherein the displacement is determined by measuring the the variation of the fluorescence intensity of the probe; and identifying a biomimetic compound of paclitaxel, wherein the biomimetic compound is identified by a drop in anisotropy of the fluorescence of the probe (page 26265, 2nd column, *Kinetics of Binding and Dissociation of Fluorescent Taxoids to Microtubules*, page 26267, 1st column and Figure 1). With regards to the microtubules, the reference teaches cross-linked microtubules

assembled in vitro in GAB and preserved with glutaraldehyde, wherein the cross-linked microtubules were found to be stable against low temperatures and dilution (page 26266, 2nd column, Preparation of Cross-linked Microtubules). With regards to the probe, Diaz et al. teach two fluorescence taxoids, 7-*O*-[*N*-(4'-fluoresceincarbonyl)-L-alanyl]Taxol (Flutax-1) and 7-*O*-[*N*-(2,7-difluoro-4'-fluoresceincarbonyl)-L-alanyl]Taxol (Flutax-2) which bind to microtubules with high affinity (abstract). With regards to antitumor substance, e.g., a test substance, which binds to the paclitaxel binding site of microtubules, the reference teaches that docetaxel was used for displacing the fluorescent probes due to it ability to bind to the Taxol binding site and larger solubility (page 26267, 1st column, paragraph bridging page 26266). Moreover, the reference teaches that the fluorescence anisotropy of the samples was measured using a Spex spectroflurometer plate reader (page 26266, 2nd column, 4th full paragraph). Thus, while Diaz et al. do not explicitly teach the preambles recited in claims 13-18 which utilize the steps of the method of claim 1, a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. (emphasis added) See In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). In addition, although Diaz et al. do not explicitly teach that the microtubules are conserved indefinitely in liquid nitrogen following dialysis against a conservation and cryopreservation buffer, the claimed limitation does not appear to result in a manipulative difference between the prior art microtubules stabilized by means of cross-linking. In the instant situation, the office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

In response to this rejection, Applicants assert that the present claims recite a second step of "determining the displacement equilibrium curve....". As such, Applicants assert that Diaz et al. does not teach or suggest how to detect a small amount of any chemically unrelated biomimetic in a

problem solution by anisotropy, nor a method of determining the binding constant of a competitor by the competitor induced Flutax displacement at equilibrium, exemplified in Figure 2 of the specification. Moreover, Applicants assert that the features concerning the microtubules used in the present invention of claim 2 are novel and were not described in Diaz et al.. In particular, Applicants assert that the microtubules of the present invention have been assembled in vitro by the method described, however, their long-term preservation was not, see paragraphs 0012 and 0030 of the specification. In particular, Applicants assert that the microtubules obtained by Diaz et al. are stable only for a few hours at the temperature necessary for the test, rendering them not susceptible for being used in large scale tests.

These arguments have been carefully considered, but are not found persuasive.

With respect to the Applicants assertions with respect to currently amended claim 1, the Examiner acknowledges that claim 1 has been amended to recite "determining the displacement equilibrium curve". However, the Examiner recognizes, as stated below, the phrase "displacement equilibrium curve" in claim 1 is a relative term which renders the claim indefinite. The phrase "displacement equilibrium curve" is not defined by the claim and the specification does not provide a standard for ascertaining the requisite degree which is encompassed by the phrase "displacement equilibrium curve". Thus, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. As such, the claim is interpreted as determining a displacement curve for prior art purposes which is clearly taught by Diaz on page 26267, 1st column and Figure 1. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., determining the binding constant of a competitor as exemplified in Figure 2 of the specification) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). With regards to Applicants arguments pertaining to the microtubules, the Examiner acknowledges, as stated above, that Diaz et al. does not explicitly teach the long term storage of the microtubules. However, the Examiner recognizes that there does not appear to be a patentably difference between the microtubules used in the present invention and those used by the prior art because, as stated by Applicants (Remarks page 8, 1st full paragraph), the microtubules of the present invention have been assembled by the method described. As such, the microtubules of

the present invention appear to be the same as those taught by Diaz et al. because they were both assembled by the in vitro method taught by Diaz et al. Along the same lines, while Applicants offer their opinion that the microtubules described by Diaz et al. are stable for only a few hours at the temperature necessary for the test, the Examiner recognizes this is only an opinion which has not been supported with any factual evidence. In the instant case, the office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claims 1-2, 4-5, 7-8, 10-11 and 13-18 remain rejected under 35 U.S.C. 102(b) as being anticipated by Andreu et al. (Biochemistry 2001; 40: 11975-11984, *IDS*).

(Note: Due to the indefiniteness of the phrase "displacement equilibrium curve" in claim 1, the claim will be interpreted as determining a displacement curve.)

Andrue et al. teach a method of providing a homogenous test for the detection of an antitumor substance in the paclitaxel binding site of microtubules, wherein said method is based on the combination of a target and a probe and comprises the following steps: adding a test substance or test substances to a solution of a target consisting of microtubules and a fluorescent probe bound to the target; determining the displacement curve of the probe from the target by the test substance, wherein the displacement is determined by measuring the drop in anisotropy via the variation of the fluorescence intensity of the probe and the resonance energy transfer to the probe bound to a suitable acceptor; and identifying a biomimetic compound of paclitaxel, wherein the biomimetic compound is identified by a drop in anisotropy of the fluorescence of the probe (entire document, specifically, page 11976, 2nd column, 1st full paragraph and page 11979, 2nd column, *Competitive Fluorescent Assay of Ligand Binding to Microtubules Measures the Binding of Taxol and Baccatin III,* and page 11980, Figure 4). With regards to the microtubules, the reference teaches cross-linked microtubules assembled in vitro and indefinitely conserved by means of dialysis against a conservation and cryopreservation buffer followed by drop-freezing into liquid nitrogen (page 11976, 1st Column,

Cross-Linked Microtubule and page 11982, 2nd column, 1st full paragraph). With regards to the probe, Andrue et al. teach that the probe includes 7-*O*-[*N*-(2,7-difluoro-4'-fluoresceincarbonyl)-L-alanyl]Taxol (abstract). With regards to antitumor substance, e.g., a test substance, which binds to the paclitaxel binding site of microtubules, the reference teaches that docetaxel and baccatin III recognizes the Taxol binding site of microtubules (page 11979, 2nd column, *Competitive Fluorescent Assay of Ligand Binding to Microtubules Measures the Binding of Taxol and Baccatin III*). Moreover, the reference teaches that the fluorescence anisotropy of the samples was screened in 96-well plates using a microplate reader (page 11979, 2nd column, 1st full paragraph). Andrue et al. further teach that the method can be used to screen for Taxol mimetics such as evaluating the binding affinity of newly designed compounds of the Taxol, epothilone, eleutherobin and discodermolide familes, as well as measuring the active Taxol-like contents of natural sources (page 11981, 2nd column, *Potential Uses of Fluorescence Anisotropy Multiwell Plate Assay in Comparison with Other Methods To Screen for Taxol Mimetics*). Thus, while Diaz et al. do not explicitly teach the preambles recited in claims 13-18 comprising the steps of the method of claim 1, a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. (emphasis added) See In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

New Rejections Necessitated by Amendment:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 4-5, 7-8, 10-11 and 13-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "displacement equilibrium curve" in claim 1 is a relative term which renders the claim indefinite. The phrase "displacement equilibrium curve" is not defined by the claim and the

specification does not provide a standard for ascertaining the requisite degree which is encompassed by the phrase "displacement equilibrium curve". Thus, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For prior art purposes, the claims will be interpreted as determining a displacement curve.

Claim 1 recites the limitation "the biomimetic compound" in step "2" of claim 1. There is insufficient antecedent basis for this limitation in the preamble or steps "1" and "2" of claim 1.

Claim 1 recites in step "2" an active step of determining the displacement equilibrium curve of the probe from the target by any test substance, wherein the biomimetic compound is identified by measuing a drop in anisotropy at varying test substance concentrations, or the variation of fluorescence intensity of the probe, or the resonance energy transfer of the probe to a suitable acceptor; and further, recites in step "3" an active step of identifying a biomimetic compound of paclitaxel, wherein the biomimetic compound is identified by a drop in anisotropy of the fluorescence of the probe or by means of a drop in resonance energy transfer to the probe bound to a ligand. Thus, claim 1 recites two active steps of identification, which renders the claim indefinite. For prior art purposes, the claims will be interpreted as using any of the identification techniques recited in steps "2" or "3".

Claims 1-2, 4-5, 7-8, 10-11 and 13-18 are further rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: a drop in anisotropy and what is being measured in step "2" of the claimed method. For example, Merriam-Webster defines anisotropy as exhibiting properties with different values when measured in different directions. Thus, while in this case the value could be presented as the concentrations, the claims do not appear to define what the "property" is. For prior art purposes, the claims will be interpreted as measuring the drop in anisotropy in the variation of fluorescence intensity of the probe.

Claims 1-2, 4-5, 7-8, 10-11 and 13-18 are further rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a correlation between the determining step and the identification step. In the instant case, it is unclear how determining a displacement equilibrium curve can be used to identify a biomimetic compound of paclitaxel.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-5, 7-8, 10-11 and 13-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

Claim 1 has been amended to recite "determining the displacement equilibrium curve of the probe from the target by any test substance." Applicants assert that support for the limitation "determining the displacement equilibrium curve" can be found in paragraphs [0013], [0014] and [0026], and Figure 2 of the specification (see Remarks, page 7). However, a careful review of the originally filed specification and claims, as well as the paragraphs and figures pointed to by Applicants, does not appear to lend support for this limitation. For example, paragraphs [0013] and [0014] describe substance which can be tested in the instant method, as well as, how to detect a competitor substance, e.g., by drop in fluorescence anisotropy of the probe (referenced ligand). However, these paragraphs do not appear to describe determining a displacement equilibrium curve. In addition, paragraph [0026] describes a fluorescence micrograph of a typical reaction mixture used in the invention and Figure 2 describes the fluorescence anisotropy of multiple solutions of 50nM Flutax-2 and binding sites of 50 nM microtubules with various concentrations of competitors (see paragraph 0027 of the specification). Yet, paragraph [0026] and Figure 2 do not appear to lend support for the limitation "determining the displacement equilibrium curve". As such, Applicant is required to cancel the new matter in the response to this Office Action. Alternatively, applicant is invited to provide sufficient written support for the "limitation" indicated above. See MPEP 714.02 and 2163.06

Claims 1-2, 4-5, 7-8, 10-11 and 13-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was

not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the nature of the invention, (2) the relative skill of those in the art, (3) the breadth of the claims, (4) the amount or direction or guidance presented, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the state of the prior art, and (8) the predictability or unpredictability of the art.

Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In Wands, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406) Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed

invention with additional experimentation, however, would render the additional experimentation undue.

The nature of the invention

The claims are drawn to an in vitro test for determining a compound which can act as a substitute for paclitaxel in the paclitaxel binding site of microtubules.

Level of skill in the art

The level of skill in the art is deemed to be high, generally that of a PhD.

The breadth of the claims

Applicants broadly claim a method of providing a homogeneous test for the detection of any antitumor substance substitutive of paclitaxel in the paclitaxel binding site of microtubules comprising adding a test substance or test substances to a solution of a target consisting of microtubules and a fluorescent probe bound to the target, determining the displacement equilibrium curve of the probe from the target by any test substance, wherein the biomimetic compound is identified by measuring the drop in anisotropy at varying test substance concentrations, or the variation of fluorescence intensity of the probe, or the resonance energy transfer of the probe to a suitable acceptor, and identifying a biomimetic compound of paclitaxel, wherein the biomimetic compound is identified by a drop in anisotropy of the fluorescence of the probe or by means of the drop in resonance energy transfer to the probe bound to a ligand. Thus, the claims encompass three active steps of contacting, determining, and identifying a biomimetic compound of paclitaxel.

Guidance in the specification and Working Examples

The specification teaches that the objection of the present method is based on the combination of the target, which consists of microtubules assembled in vitro and stabilized by means of chemical cross linking, and the probe which consists of fluoresceinated derivatives of paclitaxel, which are specifically bound to microtubules (paragraph 0012). In particular, the specification teaches that the when the probe is bound to the target it possess a much greater

fluorescence anisotropy value than that of the free probe, wherein the displacement of the probe with the target with any competitor substance can be detected by means of the drop in fluorescence anisotropy of the probe or by the drop in the resonance energy transfer (RET) or by the chance in fluorescence intensity of the probe (paragraph 0014). The specification further provides validation of the probe to target by measuring the fluorescence anisotropy (page 7) and energy transfer (page 8). Thus, while the specification clearly teaches determining the displacement of the probe by measuring the drop in fluorescence anisotropy of the probe or by the drop in the resonance energy transfer (RET) or by the chance in fluorescence intensity of the probe (paragraph 0014), the specification does not appear describe what a displacement equilibrium curve is or how to determine a displacement equilibrium curve.

Quantity of experimentation

The quantity of experimentation is extremely large given the fact that the specification, as well the prior art, does not appear to teach what a displacement equilibrium curve is or how to determine one.

Conclusion

Thus, given the lack of guidance provided in the specification for determining a displacement equilibrium curve, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as written.

All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.

Conclusion

NO claim is allowed

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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